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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/994,657	11/28/2001	Sophie E. V. Martin	56297-5016-01	8313

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EXAMINER

TUNG, JOYCE

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 03/27/2003

60

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/994,657

Applicant(s)
Martin et al.

Examiner
Joyce Tung

Art Unit
1637



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Dec 19, 2002
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above, claim(s) 13-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claims 1-21 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 1-12 in Paper No. 9 is acknowledged. Although the response indicates the election with traverse, there is no specific argument that Group I and Group II are required to be examined together. Thus, the election is treated as the election without traverse.

2. Claims 13-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group II, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for applying a voltage of not more than 50 volts to bacterial cells to release intracellular material from the cells with 2 to 5 minutes pulse duration (See pg. 15, example 1), does not reasonably provide enablement for applying a voltage of not more than 50 volts to any kinds of cells without any given duration of pulse except that there is an example that the voltage between 2V to 6V was applied to *E.coli* for 2 to 5 minutes to release protein from cells (See pg. 15, example 1). The specification does not enable any person skilled in the art to which

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it pertains, or with which it is most nearly connected, to carry out or make the invention commensurate in scope with these claims.

In Exparte Forman, 230 USPQ 546 (Bd. App. 1986), the Board considered the issue of enablement in molecular biology. The Board summarized eight factors to be considered in a determination of “undue experimentation”. These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering these factors: (a) in order to practice the invention, the practitioner must be able to apply a voltage of not more than 50 volts to any kinds of cells with any durations of pulses except of bacterial cells as described in the specification, (b) the specification provides guidance only with regard to that the voltage between 2V to 6V was applied to *E.coli* for 2 to 5 minutes to release protein from cells (See pg. 15, example 1) ; (c) working examples are presented only with regard to that the voltage between 2V to 6V was applied to *E.coli* for 2 to 5 minutes to release protein from cells (See pg. 15, example 1); (d) the invention is directed to applying a voltage of not more than 50 volts to any kinds of cells to release intracellular material (See claim 1) without any given durations of pulses; (e) the prior art of the reference Dower et al. teaches electroporation of prokaryotic cells to permeate the cells walls with the electric field strength

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5kV/cm for 2 to 20 msec and macromolecules is obtained for the cells during this period of cell wall permeability and the reference of Brodelius et al. teach applying electroporation to permeabilize plant cells for product release (See pg. 186, the Abstract) between the electric field strength 0.3 and 15kVcm⁻¹ and the pulses were 3 or 10 in which the capacitance was varied between 10 and 40 nF in some experiments in order to obtain exponential decay constants for the pulse of between 6μsec and 23μsec (See pg. pg. 186, column 2, third paragraph); (f) the level of skill in molecular biology is high; (g) the results of experiments involving applying a voltage of not more than 50 volts to any kinds of cells without specifying the durations of pulses is not predictable; (h) the claims are broadly reciting applying a voltage of not more than 50 volts to any kinds of cells without specifying the durations of pulses. Based on the above analysis, one of ordinary skill in the art would be subject to undue experimentation in applying a voltage of not more than 50 volts to any kinds of cells with any given durations of pulses.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 12 fails to particularly point out and distinctly claim the subject matter which applicant regards as the invention because the phrase "a said period" is both vague and indefinite.

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It is unclear whether the phrase refers to the "period of at least 2 minutes in claim 11 or the period of at least 30 seconds in claim 10. Furthermore, there is no distinction seen between either period and the limitation in claim 12 of "continuously" as the limitations of "at least" in both claims 10 and 11 would apply continuous current. Clarification is required.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7 Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dower. (5,186,800).

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Dower discloses the method of the present invention is used to collect intracellular substances released from cells (See column 5, lines 21-25). The method is effective with wide variety of prokaryotic cells including both gram-positive and gram-negative bacterial cells (See column 4, lines 9-57).

Dower discussed how the electrical conductivity of the medium or solution and the cell density are affecting on the electrical field (See column 4, lines 58-68 to column 5, lines 1-20). Conveniently, a non-conductive medium, such as water or sucrose is used for suspending the cells (See column 5, lines 19-20).

Dower also disclose that interelectrode spacing is critical in that it determines the electric field strength to which sample is exposed. (See column 6, lines 50-59). Usually, the electrode space is below 2.5 mm, preferably being in the range from 1.0mm to 2.0 mm (See column 6, lines 47-50) as recited in claim 7.

Dower further discussed the reason to choose a precise electric field strength based upon the cellular dimensions, for example, smaller size bacterial, the voltage 10-15kV/cm is applied and larger size bacterial, the voltage 5 to 10 kV/cm is applied (See column 7, lines 44-52).

Moreover, Dower discussed the duration applied cross the electrodes to promote the permeability of the cell wall. The precise voltage and pulse duration selected is depend on the nature of prokaryotic cell being treated. The pulse duration is generally be in the range from 2-20 sec or longer being in range from 3 to 10 sec (See column 8, lines 10-37).

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Finally, Dower indicates that the type of pulse waveform provided by the pulse generator is not critical (See column 7, lines 53-57).

Dower does not disclose applying the voltage not more than 50 volts including the range of the voltage between 0.5-50volts, the spacing between two electrodes is no more than 5mm or 10mm and the period for applying voltage is at least 30 seconds or 2 minutes continuously.

However, based upon the discussion of the factors which affects the permeability of the bacterial cells in the teachings of Dower it would have been prima facie obvious for one of ordinary skill in the art at the time of the instant invention to apply the electroporation of Dower to release intracellular material from bacterial cells with the optimization of the amount of volts, the space between two electrodes and the time needed for the pulse. The motivation is as follows: the cells are subjected to an electric field under particular conditions which render cell wall permeable to macromolecules (See column 3, lines 63-68) and the conditions include the different type of cells has different cell walls (See column 4, lines 9-17); the electric conductivity of the medium or suspension, spacing between two electrodes and the duration of the electrical field. and these parameters as discussed by Dower would have been taken into consideration by one of ordinary skilled at the time of the instant invention. Thus it would have been prima facie obvious to apply the voltage not more that 50 volts to release intracellular material from bacterial cells.

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8. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

9 Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

3.T
March 11, 2003


GARY BENZION, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600